

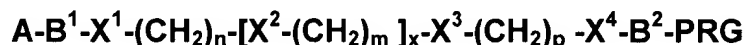
Listing of the claims

1. (previously presented) A reagent for mass spectrometric analysis of proteins which has the general formula:



where A is an affinity label that selectively binds to a capture reagent, L is a linker group which is differentially labeled with stable isotopes and PRG is a protein reactive group that selectively reacts with protein functional groups.

2. (original) The reagent of claim 1 wherein PRG is a sulfhydryl reactive group or an amine reactive group.
3. (original) The reagent of claim 1 wherein PRG is an enzyme substrate.
4. (original) The reagent of claim 1 wherein the A-L-PRG is soluble in a sample liquid to be analyzed.
5. (original) The reagent of claim 1 wherein the linker is a cleavable linker.
6. (previously presented) The reagent of claim 1 which has the general formula:



where: A is the affinity label;

PRG is the protein reactive group; and

$\text{B}^1\text{-X}^1\text{-(CH}_2\text{)}_n\text{[X}^2\text{-(CH}_2\text{)}_m\text{]}_x\text{-X}^3\text{-(CH}_2\text{)}_p\text{-X}^4\text{-B}^2$ is the linker group wherein:

X^1 , X^2 , X^3 and X^4 , independently of one another, and X^2 independently of other X^2 , can be selected from the group consisting of O, S, NH, NR, NRR^+ , CO,

COO, COS, S-S, SO, SO₂, CO-NR', CS-NR', Si-O, and aryl or diaryl groups or X¹-X⁴ may be absent;

B¹ and B², independently of one another, are optional groups selected from COO, CO, CO-NR', CS-NR', (CH₂)_q-CONR', (CH₂)_q-CS-NR', or (CH₂)_q;

n, m, p, q and x are whole numbers that can take values from 0 to about 100, where the sum of n+xm+p+q is less than about 100;

R is an alkyl, alkenyl, alkynyl, alkoxy or an aryl group that is optionally substituted with one or more alkyl, alkenyl, alkynyl, or alkoxy groups; and

R' is a hydrogen, an alkyl, alkenyl, alkynyl, alkoxy or an aryl group that is optionally substituted with one or more alkyl, alkenyl, alkynyl, or alkoxy groups

wherein one or more of the CH₂ groups in the linker can be optionally substituted with alkyl, alkenyl, alkoxy groups, an aryl group that is optionally substituted with one or more alkyl, alkenyl, alkynyl, or alkoxy groups, an acidic group, a basic group or a group carrying a permanent positive or negative charge; wherein one or more single bonds linking non-adjacent CH₂ groups in the linker can be replaced with a double or a triple bond and wherein one or more of the atoms in the linker can be substituted with a stable isotope.

7. (original) The reagent of claim 1 wherein the affinity label is biotin or a modified biotin.
8. (previously presented) The reagent of claim 1 wherein the affinity label is selected from the group consisting of a 1,2-diol, glutathione, maltose, a nitrilotriacetic acid group, and an oligohistidine.
9. (original) The reagent of claim 1 wherein the affinity label is a hapten.
10. (original) The reagent of claim 1 wherein PRG is a sulfhydryl-reactive group.

11. (original) The reagent of claim 1 wherein PRG is an iodoacetylamine group, an epoxide, an α -haloacyl group, a nitriles, a sulfonated alkyl, an aryl thiols or a maleimide.
12. (original) The reagent of claim 1 wherein PRG is an amine reactive group, a group that reacts with a homoserine lactone or a group that reacts with carboxylic acid group.
13. (currently amended) The reagent of claim 1 wherein PRG is selected from the groups consisting of a an amine reactive pentafluorophenyl ester group, an amine reactive N-hydroxy succinimide ester group, sulfonyl halide, isocyanate, isothiocyanate, active ester, tetrafluorophenyl ester, an acid halide, and an acid anhydride; a homoserine lactone reactive primary amine group, and a carboxylic acid reactive amine, alcohols or 2,3,5,6-tetrafluorophenyl trifluoroacetate.
14. (currently amended) The reagent of claim 1 wherein PRG is a substrate for an enzyme a deficiency of which is associated with a disease state.
15. (previously presented) The reagent of claim 1 wherein PRG is a substrate for an enzyme a deficiency of which is associated with a birth defect.
16. (previously presented) The reagent of-claim 1 wherein PRG is a substrate for an enzyme a deficiency of which is associated with a lysosomal storage disease.
17. (previously presented) The reagent of claim 1 wherein PRG is a substrate for acid sphingomyelinase, galactocerebroside β -galactosidase, β -galactosidase, acetyl- α -D-glucosaminidase, heparan sulfamidase, acetyl-CoA- α -D-glucosaminide N-acetyltransferase or N-acetylglucosamine-6-sulfatase.

18. (currently amended) The reagent of ~~claim 1~~ claim 6 wherein at least one of B¹ or B² is CO-NR' or CS-NR.
19. (currently amended) The reagent of ~~claim 1~~ claim 6 wherein X¹ and X⁴ are selected from NH, NR, and NRR'⁺, X³ is O and all X² groups are O.
20. (original) The reagent of claim 1 wherein the linker contains a disulfide group.
21. (original) The reagent of claim 1 wherein any atom of the linker may be substituted with a heavy isotope.
22. (original) A reagent kit for the analysis of proteins by mass spectral analysis that comprises a reagent of claim 1.
23. (original) The reagent kit of claim 22 that comprises one or more reagents of claim 1.
24. (original) The reagent kit of claim 22 further comprising one or more proteolytic enzymes for use in digestion of affinity tagged proteins.
25. (original) The reagent kit of claim 22 which comprises a set of substantially chemically identical differentially labeled affinity tagged reagents.
26. (original) The reagent kit of claim 22 wherein the reagent is an affinity tagged enzyme substrate reagent.
27. (original) The reagent kit of claim 26 which comprises a set of substantially chemically identical differentially labeled affinity tagged enzyme substrates.
28. (original) The reagent kit of claim 27 further comprising a set of substantially chemically identical differentially labeled affinity tagged enzyme products.

29. (newly added) The reagent kit of claim 22 wherein the PGR of the reagent is an enzyme substrate.
30. (newly added) The reagent kit of claim 22 wherein the PRG of the reagent is a sulfhydryl reactive group or an amine reactive group.
31. (newly added) The reagent kit of claim 22 wherein the linker of the reagent is a cleavable linker.
32. (newly added) A reagent kit for the analysis of proteins by mass spectral analysis that comprises a reagent of claim 6.